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Original Article

A comprehensive rehabilitation program improves disease severity in patients with obstructive sleep apnea syndrome: a pilot randomized controlled study

M. Desplan [a,b,c,d,*], J. Mercier [a,b], M. Sabaté [c], G. Ninot [e], C. Prefaut [a,b], Y. Dauvilliers [d,f]

[a] Université MONTPELLIER 1 and INSERM, U1046 "Physiology and Experimental Medicine of Heart and Muscle", Montpellier, France
[b] Clinical Physiology, CHU Montpellier, Montpellier, France
[c] Clinique du souffle "La Solane", Avenue des casteillets, 66230 Osseja, France
[d] Department of Neurology, Hôpital Gui de Chauliac, CHU Montpellier, National Reference Network for Orphan Diseases (Narcolepsy), France
[e] Université MONTPELLIER 1, Laboratory Epsylon, EA4556 Dynamics of Human Abilities and Health Behaviors, Montpellier F-34000, France
[f] Inserm U1061, Montpellier, France

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ABSTRACT

Background: Exercise training may improve components of metabolic syndrome and obstructive sleep apnea syndrome (OSAS). The objective of our pilot randomized controlled study was to determine the benefits of a short intensive inpatient individualized exercise training (IET) program in sedentary untreated OSAS patients.

Methods: Twenty-two sedentary patients with moderate to severe OSAS were randomly assigned either to one-month education activity sessions ($n = 11$; control group) or to inpatient rehabilitation program ($n = 11$), including IET, education activities sessions, and dietary management. Full polysomnography (PSG), OSLER (Oxford Sleep Resistance test), body composition, anthropometric measurements, metabolic syndrome components, and questionnaires were performed at baseline and at study end point.

Results: No changes occurred in the control group in all variables. Compared to controls, participants randomized to the IET group presented a significant decrease in apnea–hypopnea index (AHI) (40.6 ± 19.4 vs 28.0 ± 19.3; $P < 0.001$), oxygen desaturation index (ODI), and arousal index, which occurred in conjunction with significant decrease in body mass index (BMI), neck circumference, fat mass, fasting glucose, and diastolic blood pressure. Increased sleep latency was found in participants in the IET group with altered values at baseline.

Conclusions: IET reduced OSAS severity with improvement of metabolic syndrome components with concomitant loss in body fat in sedentary adults. If confirmed on a larger scale, a comprehensive rehabilitation program could constitute an additional or alternative treatment for moderate to severe OSAS patients.

1. Introduction

Obstructive sleep apnea syndrome (OSAS) is a prevalent sleep disorder particularly among middle-aged obese men with potential serious consequences if left untreated, including cardiovascular diseases, diabetes mellitus (DM), and metabolic syndrome [1–3]. Sedentary life leads to visceral fat accumulation, type 2 DM, metabolic syndrome, OSAS [4]. Exercise training is an effective therapy to reduce abdominal fat [5], to prevent [6] or treat type 2 DM [7], and to improve cardiovascular compartments and exercise capacity [8]. The protective association between physical activity and sleep–disordered breathing has been reported in some clinically based studies [9,10], but it also has recently been reported in a population-based longitudinal study showing a reduced incidence of mild to moderate OSAS after exercise and a worsening of OSAS after decreasing exercise [4]. Only two randomized interventional controlled trials (RCT) evaluated a non-individualized exercise program consisting of aerobic exercises in mild to moderate OSAS [11,12], with results showing an improvement in apnea–hypopnea index (AHI), slow-wave sleep, and sleep quality [12]. However, no

* Corresponding author at: CHU Montpellier, Service central de Physiologie Clinique (CERAMM), Université Montpellier 1 and INSERM, U1046, Physiologie et Médecine Expérimentale du Coeur et des Muscles, Montpellier F-34295, France. Tel.: +33 467 338 287; fax: +33 467 338 986.
E-mail address: m-desplan@chu-montpellier.fr (M. Desplan).

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study has attempted to individualize exercise training and to measure its effects in OSAS patients.

We hypothesized that physical activity based on personalized endurance training would decrease OSAS severity in sedentary patients. Our current proof-of-concept pilot RCT was designed to determine the effects of an intensive and short (4 weeks) comprehensive inpatient rehabilitation program based on individualized exercise training (IET) associated with dietary measures, in addition to a standard education program in untreated moderate to severe OSAS patients compared to an isolated standard health education program.

2. Methods

2.1. Participants

Patients between the aged of 35 and 70 years with a recent (<1 month) diagnosis of moderate to severe untreated OSAS (AHI > 15 events/h) were enrolled in our study between November 2007 and May 2010. For severe OSAS patients, we first and clearly explained that the best treatment for OSAS was continuous positive airway pressure (CPAP). All participants were sedentary as defined by the Voorrips physical activity total score below 9.0 [13]. We excluded patients with one or more of the following conditions: body mass index (BMI) $\geqslant$40 kg/m^2, regular use of hypnotic medications, and unstable cardiovascular disease. At the time of inclusion and during the study, none of the participants were treated by CPAP or mandibular advancement. Participants from the control group were asked not to drive during the protocol. The local ethics committee (CPP Sud Mediterrannée IV) approved the study (ID-RCB: 2007-A00651-52; Trial registration: NCT01362777) and all participants gave written informed consent. None of the participants were remunerated for their participation in the study.

2.2. Design

Our study is a RCT design (Fig. 1). Participants were randomly assigned either to a 4-week outpatient standard health education program twice weekly in the Montpellier University Hospital Center, France (control group); or to a 4-week inpatient rehabilitation program (Clinique du souffle "La Solane" Osseja, France) including an individualized exercise training program (IET group), health education program, and dietary management. The IET program included 24 sessions (1 session per day; 6 sessions per week during a 4-week period) of exercise training each lasting 2 h. Each session included 15 min of warming up muscles, 45 min of cycle ergometer endurance training systematically individualized to the ventilatory threshold heart rate measured on the cardiopulmonary exercise test, 30 min of muscles reinforcement with resistance training, 15 min of stretching, and 15 min of postural and balance exercises. The IET sessions were supervised by a professional using a portable heart rate monitor (POLAR, Finland) to control training intensity as previously described [14,15]. Duration, intensity, and attendance at the sessions were recorded in a logbook. Participants from both groups were asked to keep their life habits regarding physical activity during the study period. The dietary management was only performed for the IET group. A consultation with a dietician was initiated at the beginning of the study to ensure that energy intakes were appropriate to the estimated energy expenditure during IET program according to ventilatory threshold level. Basal metabolic rate was estimated according to bioimpedancemetry measurements. No restrictive diet was prescribed in both groups. The health education program included same educational activities and themes for both groups. It aimed at giving an understanding of OSAS pathophysiology, disease management, and healthy behaviors. All tests and evaluations of the study were assessed at the same place for each group in the same conditions and with the same devices.

2.3. Polysomnography

All participants were evaluated by full polysomnography (PSG) (Cidelec; France) using the following electrophysiologic parameters: Electroencephalogram (C3-A2, C4-A1, O1-A2, O2-A1), 2 electrooculograms, submental and anterior tibial electromyogram, snoring sensor, airflow measured with oronasal thermistor, nasal pressure cannula, suprasternal pressure, thoracic and abdominal bands, electrocardiogram, position detector, oxygen saturation, and heart pulse. Moderate OSAS was defined by an AHI between 15 and 29.9 events per hour of sleep, and severe OSAS by an AHI of more than 30 events per hour. The individual who analyzed the sleep study was blinded to the group allocation. For sleep analysis and scoring of the apnea or hypopnea, we used the standardized terminology of the American Academy of Sleep Medicine Task Force [16]. Thus hypopneas were defined as a >50% decrease in amplitude in airflow signal accompanied by a $\geqslant$4% oxygen desaturation or terminated with an arousal. The oxygen desaturation index (ODI) was the number of $\geqslant$4% oxygen desaturations.

2.4. Exercise capacity

The peak oxygen uptake (VO_2peak) that represents maximal aerobic capacity was assessed using a cycle ergometer (Ergoline, GmBh) during standardized maximal incremental cardiopulmonary exercise test (Medisoft, Belgium). This test is recommended before initiating the IET to determine the ventilator threshold heart rate corresponding to 55–65% of the VO_2peak [17]. Effects on endurance capacity were assessed during an endurance cycle test by measuring time through exhaustion at 80% (TTE80%Wmax) of the maximal power reached during baseline cardiopulmonary exercise test. The TTE80%Wmax was controlled at baseline and after 4 weeks, in the same conditions, using the same ergometer. Revolution rate of cycling was maintained at 60–70 revolutions per minute[11] throughout the test. The test was stopped when the participant could not maintain >10 s 55 revolutions per minute[11] despite our incentives.

2.5. The Oxford Sleep Resistance Test

The OSLER (Oxford Sleep Resistance Test) is a behavioral test that determines the mean sleep latency [18]. The participant was asked to respond by hitting a button each time a dim light flashed. The light flashed regularly for 1 s every 3 s. The participants were instructed to remain awake in this soporific situation several times (9:30 am, 11:30 am, and 1:30 pm) during the day after PSG recording for a maximum testing time of 40 min at J1 and J28. Mean sleep latency was based on the mean of the three different time sessions. When the participant failed to respond for 21 s (i.e., seven consecutive illuminations), the test ended and it was assumed that the participant had fallen asleep.

2.6. Questionnaires

The report of excessive daytime sleepiness (EDS) was evaluated with the Epworth Sleepiness Scale (ESS) [19], sleep quality with the Pittsburgh Sleep Quality Index [20], and fatigue with the Chalder Fatigue Scale [21]. We used the Hospital Anxiety and Depression Score [22] to quantify clinically relevant anxiety or depression symptoms while Health-related Quality of Life (HRQoL) was measured with the Medical Outcomes Survey Short-Form 36-item self-administered questionnaire [23].

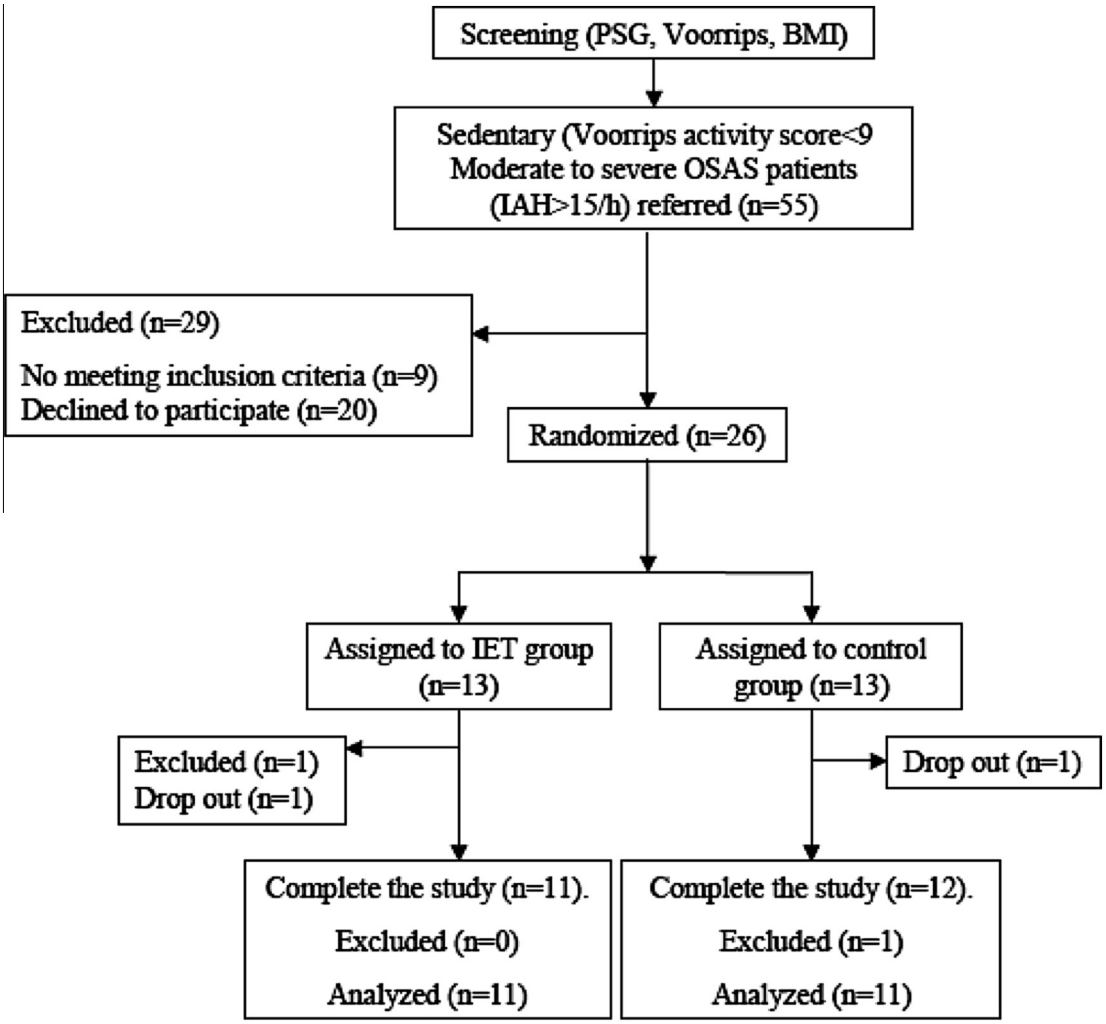

Fig. 1. Flow diagram.

2.7. Anthropometric and biologic measurements

Body composition, weight, height, and waist and neck circumferences were measured in the morning after $\geqslant$12 h of fasting. We used a multifrequency bioelectric impedance analyzer instrument (Nutriguard-M, Data Input GmbH, 64293, Darmstadt, Germany) with analysis performed with the Geneva equation [24]. A venous blood sample was obtained the morning after PSG recording to measure lipid profile and plasma glucose. The presence of a metabolic syndrome was assessed based on criteria from the International Diabetes Foundation (2005) [25].

2.8. Statistical analysis

Analyses were based on an intent-to-treat plan. In cases of dropouts, the last observations were performed for analysis. Data were analyzed with Statistica 5.0 software. Baseline characteristics of participants with OSAS according to the group assigned were compared by two-tailed unpaired *t* tests for continuous variables and a Mann–Whitney test for variables with a skewed distribution. Differences between variables measured at baseline and after 4 weeks (delta) were compared between the groups using two unpaired *t* tests for continuous variables and a Mann–Whitney test for variables with a skewed distribution. The primary outcome of interest was the delta of change in AHI between baseline and after 4 weeks in the IET program compared to the control group. A paired *t* test was also used to compare the differences in variables measured at baseline and after 4 weeks within each group. Pearson product moment correlation coefficients between AHI and fat mass, neck circumference, and endurance time to exhaustion were calculated. A value of $P < 0.05$ was considered significant.

3. Results

3.1. Participant characteristics

There were 55 participants who were referred to participate in the study with 26 participants randomized to control ($n = 13$) and IET ($n = 13$) groups, with two further exclusions and two dropouts, leading to 11 participants analyzed in each group (Fig. 1). No between-group characteristic differences were found at baseline except that ESS scores were higher in the IET group (Tables 1 and 2). None of participants experienced adverse events during the study period.

3.2. Effectiveness of the exercise training

We measured a significant improvement in VO_2peak (+3.1 mL/kg/min; +16%; $P < 0.05$) and in TTE80%Wmax (+1103 s; +265%; $P < 0.001$) for participants from the IET group compared to the control group (Table 1). Unexpectedly, we noted a slight intragroup increased TTE80%Wmax for the control group. The VO_2peak at

Table 1
Clinical and biologic sleep recording and exercise capacity data at baseline and after 4 weeks of an individualized exercise training (IET) program vs an educational program (control group) in patients with obstructive sleep apnea syndrome.

	Control group (n = 11)				IET (n = 11)			
	Baseline	After 4 weeks	p^*	$p^\#$	Baseline	After 4 weeks	p^*	$p^\dagger$
Clinical data								
BMI (kg/m^2)	31.3 ± 2.5	31.3 ± 2.2	ns	ns	29.9 ± 3.4	29.1 ± 3.1	<0.001	<0.01
Neck circumference (cm)	41.0 ± 2.5	41.5 ± 3.0	ns	ns	40.7 ± 3.5	39.2 ± 2.6	<0.01	<0.005
Waist circumference (cm)	104 (100–109)	104 (96–110)	ns	ns	99 (96–104)	96 (93–102)	<.005	ns
Lean body mass (kg)	60.1 ± 8.3	58.9 ± 6.7	ns	ns	54.9 ± 10.5	54.7 ± 9.5	ns	ns
Muscle mass (kg)	29.9 ± 5.2	29.2 ± 3.9	ns	ns	27.3 ± 7.3	27.3 ± 7.4	ns	ns
Fat mass (kg)	28.9 ± 6.5	30.2 ± 6.3	ns	ns	30.0 ± 9.4	27.8 ± 9.3	<0.01	0.005
SBP (mmHg)	128.1 ± 14.4	128.0 ± 18.2	ns	ns	141.8 ± 15.8	145.6 ± 23.2	ns	ns
DBP (mmHg)	82.5 ± 7.1	78.8 ± 9.7	ns	ns	79.0 ± 7.1	73.0 ± 10.3	<0.05	ns
Biologic data								
Triglycerides (mg/dL)	150.6 ± 47.0	152.5 ± 72.0	ns	ns	165.6 ± 89.7	106.3 ± 26.2	ns	ns
HDL cholesterol. (mg/dL)	48.7 ± 10.0	48.5 ± 11.5	ns	ns	41.8 ± 14.5	42.1 ± 6.3	ns	ns
Fasting glucose (mg/dL)	98 (93–102)	93 (88–108)	ns	ns	101 (89–111)	86 (81–98)	<0.005	<0.05
MS[**] (n)	10	8	ns	ns	10	6	<0.05	<0.05
Polysomnographic data								
TST (min)	404.4 ± 81.3	433.2 ± 61.8	ns	ns	421.5 ± 72.6	417.3 ± 81.0	ns	ns
NREM sleep (%)	79.4 ± 6.5	82.0 ± 5.4	ns	ns	81.4 ± 4.0	78.4 ± 4.1	ns	ns
Arousals/h	29.9 ± 13.7	36.6 ± 18.9	ns	ns	41.3 ± 17.5	32.3 ± 11.7	ns	<0.05
ODI/h	24.9 ± 12.4	30.1 ± 23.1	ns	ns	23.1 ± 15.8	17.6 ± 13.2	<0.01	<0.05
AHI/h	39.8 ± 19.2	45.4 ± 22.5	ns	ns	40.6 ± 19.4	28.0 ± 19.3	0.001	<0.005
Exercise capacity								
VO_2Peak (mL/kg/min)	23.2 ± 6.0	19.8 ± 4.6	ns	ns	21.3 ± 5.6	22.9 ± 5.6	<0.05	<0.05
MET (kcal/kg/h)	3.3 ± 1.7	2.91 ± 1.2	ns	ns	3.6 ± 1.9	4.6 ± 1.0	<0.01	<0.01
VT heart frequency	117 ± 20	118 ± 16	ns	ns	112 ± 18	121 ± 16.4	<0.05	<0.05
VT watt	93 ± 34	79 ± 15	ns	ns	72 ± 36	95 ± 23	<0.001	0.005
Endurance test (sec)	488 ± 338	668 ± 437	<0.05	ns	770 ± 401	1771 ± 640	<0.001	<0.001

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; MS, metabolic syndrome prevalence; TST, total sleep time; NREM, nonrapid eye movement; ODI, oxygen desaturation index; AHI, apnea–hypopnea index, IET, individualized exercise training program; VO_2Peak, peak oxygen uptake; MET, metabolic equivalent of task; VT, ventilatory threshold; Pmax, maximal power; s, seconds.

[*] Intragroup comparison before and after using paired t test for continuous variable/Mann–Whitney test if skewed distribution.

[**] MS, Metabolic Syndrome International Diabetes Foundation criteria [5]. Values are presented as mean ± standard deviation. Abdominal circumference and fasting glucose were presented as median (25–75%) due to skewed distribution.

[#] Between groups comparison for baseline characteristics using unpaired t test for continuous variable/Mann–Whitney test for variables with skewed distribution.

[†] Between groups comparison for difference between variables measured at baseline and after 4 weeks (delta) using two unpaired t tests for continuous variables.

Table 2
Sleep, fatigue, depression, and quality of life data assessed by questionnaires at baseline and after 4 weeks in patients with obstructive sleep apnea syndrome in the group with individualized exercise training programs vs educational programs (control group).

	Control group (n = 11)		p^*	IET (n = 11)		p^*
Epworth Sleepiness Scale (range 0–24)						
Score	8.0 ± 5.7	9.4 ± 5.8	0.12	13.6 ± 4.5	8.0 ± 5.7	0.002
Short-form 36 health survey (0–100)						
Physical functioning	70.0 ± 31.2	80.9 ± 16.1	0.29	72.7 ± 18.9	92.2 ± 5.8	<0.005
Role limitation (physical)	70.5 ± 36.8	70.5 ± 36.8	1.00	36.4 ± 37.7	86.4 ± 23.3	<0.005
Vitality	53.2 ± 15.7	52.3 ± 13.5	0.83	38.1 ± 22.9	76.2 ± 11.8	0.0002
Role limitation (emotional)	54.6 ± 40.2	60.6 ± 44.3	0.72	57.6 ± 47.4	78.8 ± 30.8	0.13
Mental health	45.9 ± 15.6	49.9 ± 17.9	0.17	56.4 ± 19.8	64.1 ± 19.0	0.20
Social functioning	66.9 ± 21.9	73.3 ± 24.7	0.19	56.7 ± 35.0	83.9 ± 12.3	0.02
Bodily pain	71.8 ± 27.4	60.1 ± 26.1	0.27	56.6 ± 30.6	77.5 ± 17.2	0.007
General health perception	54.1 ± 12.6	52.3 ± 14.0	0.63	46.4 ± 22.3	63.6 ± 9.5	0.01
Hospital Anxiety and Depression Scale (range 0–21)						
Anxiety	9.5 ± 3.5	10.4 ± 3.8	<0.05	11.4 ± 4.0	7.1 ± 3.7	0.003
Depression	8.4 ± 4.7	8.3 ± 3.6	0.93	8.3 ± 4.8	4.7 ± 2.6	0.01
Chalder Fatigue Scale (range 0–32)						
Physical fatigue	14.6 ± 3.5	17.2 ± 6.0	0.29	18.9 ± 5.6	10.8 ± 4.6	0.002
Mental fatigue	10.9 ± 4.7	10.4 ± 2.9	0.67	11.3 ± 3.2	7.4 ± 1.4	<0.005
Pittsburgh Sleep Quality Index (range 0–21)						
Score	8.0 ± 3.1	8.1 ± 3.8	0.81	8.9 ± 3.1	6.2 ± 1.5	0.01

Abbreviation: IET, individualized exercise training.

Values are presented as mean ± standard deviation.

[*] Intragroup comparison before and after: paired t test for continuous variable/Mann–Whitney test if skewed distribution.

ventilatory threshold measured during cardiopulmonary exercise test was increased by 42% in the IET group ($P < 0.001$), but no change was noted in the control group. Using this VO_2 level, we estimated that the energy expenditure would increase by 28% after 4 weeks of IET, though no significant change was found in the control group (Table 1).

3.3. Exercise training and OSAS severity

Individual values of AHI at baseline and after 4 weeks of intervention were reported in both groups (Fig. 2). Between-group comparisons for differences (delta) between AHI measured at baseline and after 4 weeks, the primary outcome of interest, showed significant results ($P < 0.005$). The AHI significantly decreased after 4 weeks for participants randomized in the IET group (from 40.6 ± 19.4 to 28.0 ± 19.3/h; $P < 0.001$), though AHI was unchanged in the control group. A response rate defined as 50% or more reduction in AHI was found in 4 out of 11 participants (36%) in the IET group and none in the control group ($P = 0.09$). A success therapy defined as 50% or more reduction in AHI plus a postrehabilitation program AHI of less than 15 was reported in 3 out of 11 participants (27%) in the IET group and none in the control group ($P = 0.21$).

Table 1 shows secondary outcomes of the intervention on anthropomorphic, metabolic, sleep, and ventilation components after 4 weeks in both groups. The ODI and arousal index were significantly decreased after 4 weeks of IET. Participants assigned to the IET group had significantly decreased BMI, fat accumulation (fat mass), waist and neck circumference, diastolic blood pressure, and fasting glucose. Changes in AHI were correlated to the changes on fat mass and neck circumference ($r = 0.45$ and $r = 0.44$, respectively; $P < 0.05$). A significant decrease in daytime sleepiness (ESS), fatigue score, and sleep quality, together with an improvement in mood (Hospital Anxiety and Depression Score) and most HRQoL items were found after 4 weeks in the IET group, while there was no change in the control group (Table 2).

Mean sleep latency measurements by the OSLER test did not change when comparing the measures at baseline and after 4 weeks in both the control group (1794 ± 596 s vs 1671 ± 795 s) and in the IET group (1753 ± 735 vs 1821 ± 733 s). However, most of the participants ($n = 12$) showed normal baseline results (2400 s). When considering only participants with altered mean sleep latency at baseline, participants from the IET group ($n = 5$) showed an improvement of mean sleep latency (delta = +447 ± 325 s; $P = 0.04$), though no change was noted in the control group ($n = 5$; delta = −158 ± 504 s). The first OSLER session performed at 9:30 was the only one with significant mean sleep latency improvement after IET.

4. Discussion

We reported the results of a pilot RCT study which investigated the benefits of a short intensive inpatient IET program compared to a standard health education program in sedentary patients with untreated moderate to severe OSAS. We demonstrated that an intense IET program targeted to the ventilator threshold is associated with a decrease of 31% on the AHI with concomitant reduction of the ODI and arousal index, diastolic blood pressure, fasting glucose, BMI, fat mass, and waist circumference, together with increased mean sleep latency in selected participants with altered values at baseline. The report of EDS, fatigue, mood changes, quality of sleep, and HRQoL scores also showed significant improvement after the implementation of an IET program.

The gold standard therapy for severe OSAS is CPAP; however, some patients may not tolerate such treatment or with low adherence, and the positive effects of CPAP on altered metabolism status frequently associated with OSAS remain unclear [26–28]. Previous studies evaluating different types of exercise training and lifestyle intervention have been published on OSAS severity with positive results [11,12,29–31]. Two RCT studies focusing on exercise of the oropharyngeal muscle showed positive effects on AHI and subjective EDS [32,33]. Concerning whole body exercise training, two RCTs studies have also been reported with positive effects. The

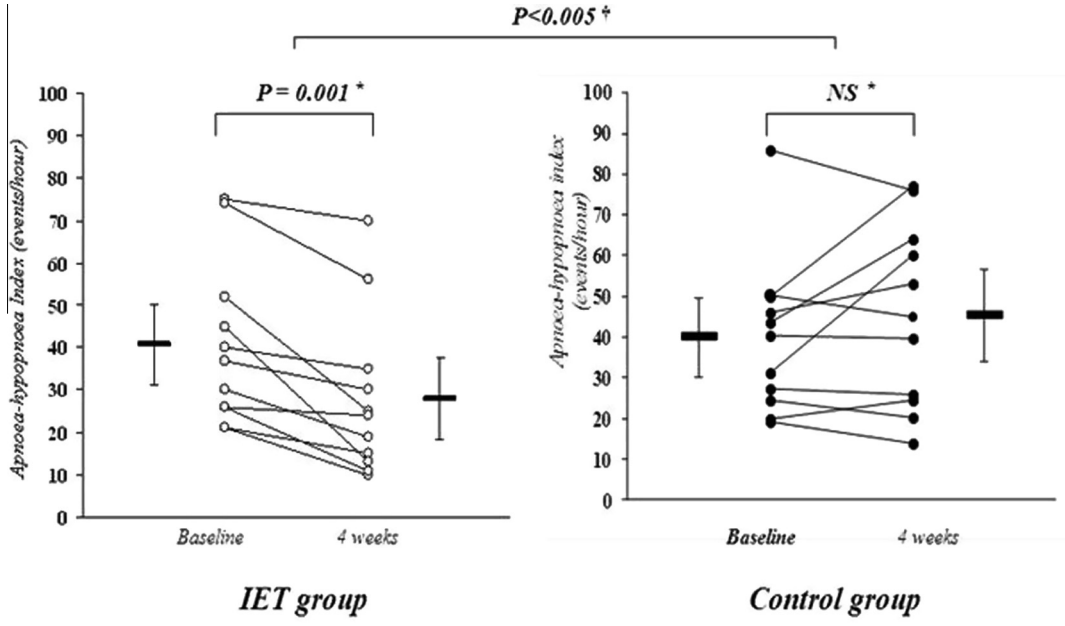

Fig. 2. Apnea–hypopnea index at baseline and after 4 weeks of an individualized exercise training program vs an educational program (control group) in patients with obstructive sleep apnea syndrome. *Abbreviations:* NS, not significant; IET, individualized exercise training. Short horizontal lines and bars are mean ± standard deviation. *Intragroup comparison before and after using paired *t* test for continuous variables. †Between groups comparison for differences between variables measured at baseline and after 4 weeks (delta) using 2 unpaired *t* tests for continuous variables.

first RCT on the effects of exercise performed at a submaximal intensity of 60–70% of VO_2peak during 1.5 h three times weekly for 12 weeks was associated with respiratory muscle training. The authors reported significant improvement in AHI severity and exercise capacity without change on daytime sleepiness measured by ESS in mild to moderate OSAS participants [11]. The second more recent RCT reported the positive effects of a 12-week exercise training program of four times per week with 150 min per week of moderate to intense aerobic activity in sedentary overweight or obese adults with moderate to severe untreated OSAS. The participants were compared to a stretching control group on variables such as AHI, ODI, stage 3 nonrapid eye movement sleep, sleep quality, fatigue, neurobehavioral performances, and body weight [12,34]. Unfortunately, the latter study did not include an IET or any measurement of the activity level to identify sedentary patients [12]. In our study, we only included participants with confirmed low physical activity (Voorrips physical activity total score below 9.0); the exercise program was carefully performed, monitored, and individualized. We used the endurance test to measure the effects of the IET program, which was considered the most appropriate measurement of the post-IET effects [35].

Our comprehensive rehabilitation program based on IET showed a significant improvement in endurance time compared to the control group, with only a modest change on VO_2peak. As previously reported, individualized exercise training at the ventilator threshold heart rate was clearly effective and safe for sedentary patients with high cardiovascular risk metabolic status [14], but it also allowed us to control intensity and to estimate energy expenditure. The rehabilitation program proposed in our study was an integrative and multidisciplinary approach known to improve exercise tolerance and dyspnea on exertion, in addition to fatigue, mood, and HRQoL in sedentary patients as described in the American Thoracic Society/European Respiratory Society statement [16]. At the end of the IET program, a decrease in 31% on the AHI was found in participants but still three patients presented severe OSAS compared to seven participants at baseline. The response rate (defined as 50% or more reduction in AHI) and the success therapy (defined as 50% or more reduction in AHI plus a postrehabilitation program AHI of less than 15 events per hour) were reported in 36% and 27% of participants in the IET group, respectively. Thus IET resulted in a moderate reduction in AHI, which may be considered as clinically nonsignificant. We also reported a significant improvement in BMI, fat mass, and metabolic syndrome components, which is in agreement with the results of previous studies reporting the benefits of exercise training on obesity, metabolic syndrome components, and type 2 DM [5–8].

The mechanisms behind the benefits of IET in sedentary patients with OSAS may be multiple and not just through weight loss. Exercise training could induce both fat loss and change in fat location, and increase pharyngeal lumen size known to be reduced due to fat deposition within the airway or in its lateral walls [36,37]. Being a rich source of humoral mediators including leptin and other inflammatory cytokines, visceral fat accumulation may impact on neural pathways associated with respiratory control leading to oropharyngeal muscle dysfunction [38,39]. Exercise training can redistribute and drain the excessive fluid from the legs that contributes to the pathogenesis of OSA [40], but it also can reverse low grade inflammation markers and leptin levels in patients with altered metabolism status [41]. Long-term exercise may also be responsible for positive effects on sleep architecture, particularly in increasing slow-wave sleep, with a decrease in AHI as a consequence [42,43].

Our pilot study has some limitations. First, the small sample size and the inpatient rehabilitation program, even on short-term duration, limit the external validity of our findings. Because sedentary OSAS patients presented frequent comorbid metabolic diseases, we decided to propose an efficient model of intensive and comprehensive rehabilitation program designed for chronic respiratory diseases [18] to reverse the global illness with several lifestyle interventions. We acknowledge that the management of the inpatients exercise group may differ from the outpatient education setting control group. Second, a longer period of training, a repetition of the parameter evaluated after a washout period, and long-term monitoring could be necessary to evaluate if the benefits of IET persist over time in the absence of further physical activity. Our proof-of-concept inpatient pilot study is an expensive trial, with further health economic cost-effectiveness evaluations required before its potential generalization. Third, the effectiveness of the IET in mild OSAS patients, in patients without any metabolic comorbidities, or in physically active patients remains unknown. Dietary and IET interventions in our study were associated with reduction in AHI and BMI with correlations between changes in AHI, fat mass, and neck circumference. Thus it was difficult to separate the effects of diet management from exercise training.

5. Conclusion

A short, intensive, multidisciplinary, and comprehensive rehabilitation program based on IET and dietary measures significantly reduced OSAS severity with concomitant loss in body fat and improvement of metabolic syndrome components in sedentary patients with moderate to severe OSAS. Further studies are required to confirm these preliminary results. A larger-scaled long-term assessment may constitute an additional or alternative treatment for improving patients with OSAS.

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Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2013.09.023.

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